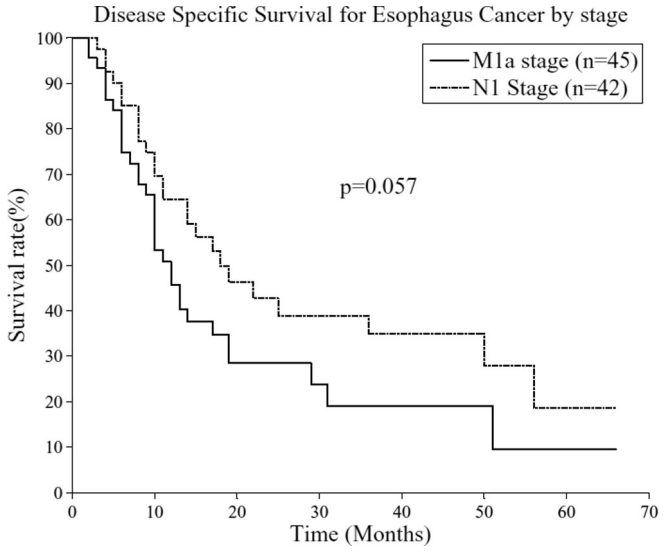

FIGURE 1. Disease-specific survival comparison for N1 versus M1a status in patients with locally advanced carcinoma of the esophagus.

M1a esophagus cancer have a poorer prognosis than patients with M0 disease.

We would like to thank Drs. Schomas, Miller, and Quevedo for the opportunity to discuss and further clarify our data. Their letter specifically requests for additional data and comment on the nonoperative patients treated with chemoradiation. Our 2-year overall and disease-specific survival rates for patients with M1a disease were 13% and 11%, respectively, for this group.

To answer the question about a comparison of patients staged as M1a versus N1, we have included Figure 1 with this response letter. When staging M1a versus M1b disease, we followed the guidelines of the American Joint Committee on Cancer staging system. We did not attempt to differentiate stations 17 (left gastric), 18 (common hepatic), and 20 (celiac) from each other. These stations were collectively considered M1a disease for patients with lower esophagus and gastroesophageal cancers. Surgical staging can clearly distinguish these separate nodal stations. However, nodes in these stations appear similar on computed tomography imaging. Radiology reports do not and cannot clearly distinguish this difference.

The main point of this query is that patients with locally advanced esophagus cancer, even stage M1a, deserve the opportunity to receive definitive therapy because a few of them can be cured by this approach, especially if they fit within the highly selective category of operative patients. First, we only had 10 patients with M1a disease who underwent esophagectomy. These tended to be younger patients without medical comorbidities who were fit enough to receive trimodality therapy. Most received chemoradiation alone. We certainly agree that chemoradiation can cure a few patients with locally advanced esophageal cancer. However, our survival outcomes with nonoperative therapy for patients with M1a disease clearly fall into the "dismal" category. Although 13% of our patients survived 2 years, almost all the remaining patients died of their esophagus cancer. For them, the treatment was largely palliative. Clearly, newer innovative therapy is needed for this dreaded disease.

The treatment options for patients with locally advanced esophagus cancer have not changed since the 1980s. Radiation Therapy Oncology Group 8501, initiated in 1986, used cisplatin, 5-FU, and 50 Gy in the chemoradiation arm of this trial for inoperable patients.[2] For operable patients, a randomized trial published by Walsh et al.[3] used cisplatin, 5-FU, and 40 Gy preoperatively. With the exception of some minor variations in radiation technique, both these trials continue to drive therapy today. Newer therapies are needed if we are to improve outcome for these patients. With respect to radiation therapy, trials applying newer techniques to deliver increased doses are warranted, such as intensity modulation, image guidance, and even proton therapy. Likewise, the era of individualized therapy should apply to trials for patients with esophagus cancer, mirroring distinctions being made in therapies for lung and other aerodigestive cancers.

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Persistent Confusion on the Clinical and Pathologic Nodal Staging in Lung Cancer

To the Editor:

The answer to the last frequently asked question included in the International Association for the Study of Lung Cancer Staging Manual in Thoracic Oncology (Table 1)[1] has been met with concern by the members of the Bronchogenic Carcinoma Cooper-

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TABLE 1. Frequently Asked Question and Answer[1]

Question	Clinical classification suggested that our patient had a T2 N2 M0 NSCLC. Preoperative biopsy of ipsilateral mediastinal nodes confirmed N2 disease, and a thoracotomy was not undertaken. Should this case be classified as cN2 or pN2? Should this case now be assigned a pathologic stage?
Answer	Microscopic confirmation of the nodal disease would allow this to be classified as pN2. However, to be designated a pathologic stage, the primary tumor must also have been confirmed on biopsy to establish the pT category.

ative Group of the Spanish Society of Pneumology and Thoracic Surgery.

To classify as pathologic (p) N2 a tumor that has not been resected, even if there is pathologic confirmation of the metastatic nature of the lymph nodes by means of any preoperative endoscopy (transbronchial needle aspiration, ultrasonography-assisted bronchoscopy, or oesophagoscopy with fine needle aspiration), percutaneous needle aspiration, or surgical exploration (mediastinoscopy, mediastinotomy, extended cervical mediastinoscopy, or thoracoscopy) goes against general rule 2 of the tumor (T), node (N), metastasis (M) classification of malignant tumors, which says "Clinical classification (. . .) is based on evidence acquired before treatment. Such evidence arises from physical examination, imaging, endoscopy, biopsy, surgical exploration, and other relevant examinations."[2] "Pathologic classification (. . .) is based on the evidence acquired before treatment, supplemented or modified by the additional evidence acquired from surgery and from pathologic examination (. . .)" and "entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category (. . .)" and "the removal of nodes (. . .)." "An excisional biopsy alone of a lymph node without pathologic assessment of the primary is insufficient to fully evaluate the pN category and is a clinical classification (. . .)."[2]

Back, at least, to the early 1990s, some chest physicians and oncologists, mainly in North America, started to think that pathologic confirmation of tumor extent in the pretreatment assessment of lung cancer entitled them to assign a pathologic classification to these tumors. This is an evident misinterpretation of the word "pathologic" in the context of the TNM classification and a violation of the general rule 2. This misinterpretation eventually found its way into medical writing, as we pointed out in 2004.[3] Now, 5 years later, this schismatic use of the "p" prefix seems to be explicitly sanctioned by the International Association for the Study of Lung Cancer.

There are important implications associated with this misunderstanding that go beyond mere taxonomy. According to the general rules, even if a cytohistologically diagnosed tumor has pathologic evidence of nodal disease, its classification will still be clinical by definition, because the tumor has not been resected. If we assign "p" status to tumors that have not been resected, we will be mixing tumors with very different prognosis, i.e., tumors with pathologic confirmation of their anatomic extent but that do not undergo resection and tumors that have been resected and have a proper pathologic classification. The Certainty Factor[4] offers the possibility to code in a different way those nodes considered involved by imaging methods and by pathologic confirmation in the clinical phase of the tumor classification without relying to the "p" prefix, which should be reserved for pathologic classification, only.

In conclusion, assigning "p" status to unresected tumors that have pathologic confirmation of their nodal extent goes against general rule 2 of the TNM classification; it produces a mixture of cases of different prognosis that undermines the prognostic capacity of the TNM classification for lung cancer gained by the revisions that lead to its 7th edition, and therefore, it should be avoided.

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In Response:

We are grateful to the editor for an opportunity to respond to this question, which it is proposed to publish in the *Journal of Thoracic Oncology*. We should emphasize that the chapters in the *IASLC Manual on Thoracic Staging*[1] to which the comments are addressed, and many other chapters in this book, and the companion *IASLC Handbook of Staging in Thoracic Oncology*,[2] were reproduced with the permission of the International Union Against Cancer from publications to be published later this year: the *TNM Classification of Malignant Tumors* 7th edition and the *TNM Supplement: A Commentary on Uniform Use* 4th edition. Fuller explanatory notes will be available in these publications.

The International Association for the Study of Lung Cancer was accorded the privilege of publishing these chapters ahead of the source material because of its central role in formulating the proposals for the 7th edition and delays in the publishing schedules of the International Union Against Cancer and the American Joint Committee on Cancer, the two bodies that administer the tumor, node, metastasis (TNM) classification worldwide. In no sense was it the

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